of selection bias (the sickest children might die before reaching one of these units), but the recent dramatic improvement in outcome in paediatric intensive care units[1] implies that it is the result of improved care and that early referral to such a unit would be likely to improve mortality.

Hospital treatment

The SIGN guidelines emphasise the need for vigorous fluid resuscitation and early intubation, for which there is no good evidence but strong consensus. For fluid-resistant shock, inotropes are recommended on the basis of case-control findings of an association between inadequate inotropes and worse outcome.[5] The SIGN recommendation to use a third generation cephalosporin to treat meningococcal infection, rather than the narrower spectrum antibiotic benzylpenicillin, is not explained but is unlikely to affect outcome.

The SIGN guidelines represent a laudable attempt to improve management. We lack high level evidence on which interventions are most likely to improve outcome, and future randomised controlled trials of interventions would be invaluable. Apart from primary prevention, major advances in improving the outcome of childhood meningococcal infection in the UK seem most likely to follow system changes to improve supervision of junior doctors in emergency departments, good access to experienced paediatricians, and early referral to specialist centres.[5]

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LESSON OF THE WEEK

Unrecognised severe vitamin D deficiency

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Vitamin D deficiency remains common and may mimic other musculoskeletal disorders or mental health problems

Since Glisson gave the first authoritative description of rickets in 1650 and McCollum and coworkers described its cause as vitamin D deficiency in 1922,[1] clinical descriptions of hypovitaminosis D have become more variable, making the condition less recognisable.[2] At the same time, the condition remains highly prevalent world wide, yet is preventable.[3] We present two cases of longstanding undiagnosed severe vitamin D deficiency with important clinical consequences.

Case reports

Case 1

A 53 year old woman of Pakistani origin underwent mastectomy for invasive ductal carcinoma of the right breast with adjuvant radiotherapy and tamoxifen treatment. Over the next two years she presented at her follow-up appointments with migratory musculoskeletal pains, including pain in the right arm, loin, right posterior chest with bony tenderness and whole body discomfort. A chest x ray showed an irregularity of the upper cortex of the right posterolateral seventh rib. An isotope bone scan showed multiple areas of increased radionuclide uptake in the ribs and left sacroiliac joint. We made a working diagnosis of metastatic bone disease and started the aromatase inhibitor anastrazole and the oral bisphosphonate sodium clodronate.

Over the next six months her pains worsened, and areas of tenderness in the arms, legs, ribs, and left sacroiliac joint were poorly controlled by cocodamol. A repeat bone scan showed no change (fig 1). A poor prognosis was given and combination chemotherapy (adriamycin, taxotene) was planned, but first she took a six week summer trip to Pakistan to visit family. On her return to the United Kingdom, her symptoms had completely resolved. A whole body computed tomography scan showed a pelvic stress fracture but no evidence of visceral metastasis. Chemotherapy was delayed.

Her symptoms relapsed during winter and spring. When pain in the left lateral ribs and right hip worsened, she was switched to a second line aromatase inhibitor, exemestane. She was also given an intravenous infusion of the aminobisphosphonate pamidronate 90 mg, after which she acutely developed distal

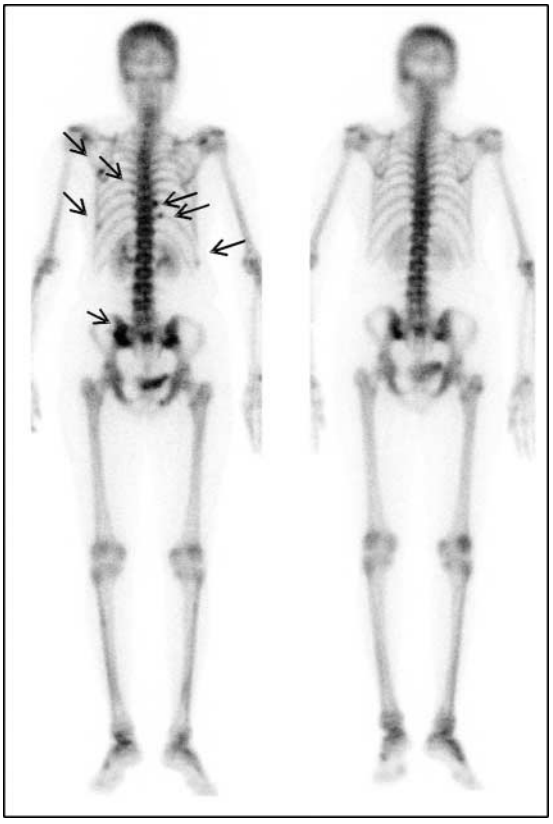

Fig 1 | Tc 99m HDP bone scan before rescue therapy with vitamin D (left) showed increased uptake of radionuclide tracer in ribs and left sacroiliac joint. After rescue therapy (right), scan showed no appreciable uptake at any sites

paraesthesiae and muscle spasms. A positive Chvostek's sign was noted along with serum corrected calcium of 1.25 mmol/l (normal range 2.12-2.60 mmol/l).

She was treated with intravenous calcium gluconate followed by oral calcium carbonate and was referred to the endocrinology service. At follow-up, her serum corrected calcium was 2.17 mmol/l and she had a raised plasma parathyroid hormone concentration of 474 ng/l (normal range 10-60 ng/l) and a serum 25-hydroxyvitamin D concentration of 19 nmol/l (local laboratory reference range 25-75 nmol/l). She had risk factors for severe hypovitaminosis D (skin pigmentation, use of traditional full-body coverings, residence at high latitude (55°N), and multiparity) and reported an aversion to consumption of dairy products. Severe vitamin D deficiency was diagnosed. Because of previous irregular follow-up and variable concordance with medication, she was treated with intramuscular cholecalciferol 300 000 U monthly and oral calcium carbonate 1 g daily.

Four years later her symptoms had entirely resolved, biochemistry was normal, and repeat isotope bone scans (fig 1) also remained normal.

Case 2

A 35 year old woman of Pakistani origin presented to her general practitioner with unexplained migratory muscle and bone pains in the middle trimester of her third pregnancy. The pain continued for six months and after the birth of her childa diagnosis of postpartum depression with somatisation was made and treatment with fluoxetine started. Her pains persisted over the next two years and were variously recorded as plantar fasciitis, muscle pain, backache, and generalised joint pain.

On assessment in the endocrine clinic, she reported increasing pains in her ribs and hip on the right, both heels, and lower abdomen. Physical examination revealed an antalgic gait with right sided hip pain, proximal myopathy, and tenderness over her right lower ribs. Several risk factors for vitamin D deficiency were identified: skin pigmentation, use of a head scarf, multiparity, and residence at 55° North latitude. She did not eat cheese, and rarely ate milk or fish, and had a history of iron deficiency anaemia.

Subsequent investigations confirmed severe vitamin D deficiency, with a corrected serum calcium of 1.89 mmol/l (normal range 2.12-2.60 mmol/l), plasma parathyroid hormone of 864 ng/l (normal range 10-60 ng/l) and 25-hydroxyvitamin D of 7 nmol/l (local laboratory reference range 25-75 nmol/l). An x ray of her pelvis showed a pseudofracture (Looser's zone) on the right lesser trochanter (fig 2). She was given oral ergocalciferol 10 000 U daily. Her daughter, 30 months old, was described as having leg deformity, and treatment with ergocalciferol drops was started after assessment.

Discussion

These cases highlight that osteomalacia secondary to severe vitamin D deficiency may remain unrecognised for many years, at one extreme staying below the clinical threshold as a migratory non-specific pain syndrome and at the other extreme mimicking metastatic bone disease and leading to a spurious indication for chemotherapy.

Similar cases are likely to become more prevalent. In the UK, nearly 90% of adults aged 45 have suboptimal concentrations of vitamin D (<75 nmol/l) in winter and spring, of whom 16% have severe vitamin D deficiency (<25 nmol/l).[4] Acknowledged as an emerging problem

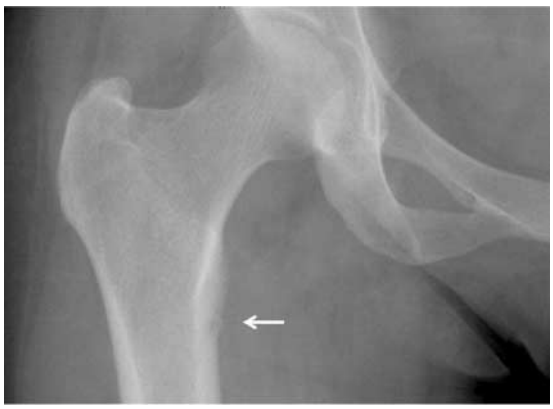

Fig 2 | Pseudofracture (white arrow) of the medial aspect of the right femur proximal to the lesser trochanter

in the South Asian community more than three decades ago,[5-7] vitamin D deficiency affects nearly all non-white residents of the UK to some degree, and 50% have severe deficiency in winter and spring.[8] Women are especially at risk for moderate to severe (<25-40 nmol/l) vitamin D deficiency.[4] The risk is fourfold for those who are multiparous and fivefold for those who are veiled.[9] Poor exposure to sunlight, higher latitude, winter season, inadequate diet, older age, obesity, and housebound status are also important risk factors.[3 4 9-13]

The high prevalence of hypovitaminosis D mandates early clinical recognition. Widespread pain, which may also be a presenting feature of affective disorders, can be a prominent manifestation in South Asians.[14 15] Pain is 3.5 times as prevalent in South Asians with severe hypovitaminosis D (<25 nmol/l) than those without in the UK.[15] But the lack of specificity complicates interpretation. Symptoms of hypovitaminosis D, including diffuse or migratory pain affecting several sites (especially the shoulder, pelvis, ribcage, and lower back) have also been misdiagnosed as physical illnesses, including fibromyalgia, polymyalgia rheumatica, and ankylosing spondylitis.[2] Associated polyarthralgias and synovitis of the hands and feet have been confused with rheumatoid arthritis and polymyositis, and myopathy with proximal weakness has been confused with amyotrophic lateral sclerosis, and pseudofractures have been misinterpreted as metastatic bone disease.[2] Although persistent, non-specific musculoskeletal pains and weakness may represent a unifying set of features,[2 3 16] this overlap with other rheumatological conditions, as well as depression, necessitates a high index of suspicion in the diagnosis of hypovitaminosis D.

Experts have called for adequate vitamin D status to be dealt with at the public health level.[17 18] Higher 25-hydroxyvitamin D thresholds have been proposed as the health sequelae of mild hypovitaminosis D deficiency have expanded beyond rickets and osteomalacia to include low bone mineral density, impaired function of the legs, fractures, admissions to nursing homes, colorectal and prostate cancer, non-Hodgkin's lymphoma, periodontal disease, type 1 diabetes, and multiple sclerosis.[3] Evidence is emerging of the epidemiological link of vitamin D deficiency to breast cancer, and also that dietary supplementation could reduce cancer risk.[19 20]. A meta-analysis of randomised controlled trials has also shown a modest reduction in all cause mortality in groups treated with vitamin D.[21]

An optimal serum concentration was recently defined as ≥75 nmol/l on the basis of several of these outcomes.[22] This higher threshold necessarily implies a revision of the current recommended intakes for vitamin D. An increase in daily vitamin D intake from 200-600 IU[23] to ≥1000 IU for all adults has been proposed, to achieve serum concentrations ≥75 nmol/l. This includes input from the primary source of vitamin D, cutaneous photosynthesis from ultraviolet B sunlight, which supplies 90% of total circulating levels in most people.[24] Achieving these vitamin D targets in the UK presents a considerable challenge—obstacles include high latitude, persistent cloud cover, office based Western lifestyles, and inadequate dietary sources of vitamin D, including a lack of food fortification[4] and suitable over the counter preparations.[4]

Guidance on screening, recommended intakes, and exposure to sunlight has not adapted to changing demographics and epidemiology. In particular, UK recommendations for exposure to sunlight may not have struck the necessary balance between preventing skin cancer and avoiding vitamin D deficiency.[25] Warnings to limit direct exposure to sunlight, seek shade, cover skin, and apply sunscreens with a protection factor of 15 or more (factor 15 blocks vitamin D photosynthesis by 99%) do not have uniform health effects across different skin colours, dress habits, or age groups.[3 18 22 24] In the absence of effective prevention strategies for severe hypovitaminosis D, clinicians must remain vigilant to its heterogeneous and potentially sinister clinical presentation.

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A PATIENT'S JOURNEY

Becoming a live kidney donor

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ANALYSIS, p 1346,
REVIEWS, pp 1377, 1378

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This is one of a series of occasional articles by patients about their experience of traumatic medical events that offer lessons to doctors. The *BMJ* welcomes contributions to the series. Please contact Peter Lapsley (plapsley@bmj.com) for guidance.

In 2007, Annabel Ferriman gave one of her kidneys to an old friend. This is the story of her journey through that process

Last year I gave one of my kidneys to an old friend, Ray, who was months away from needing dialysis because of polycystic kidney disease. The operation was a success. Ray is doing well and is back at work, and I feel completely healthy and have had no adverse effects.

It was a positive experience for both of us, but some aspects of the patient journey, in particular the endless tests leading up to the transplant, were so protracted that I was left seething with rage. I am recounting the tale partly to encourage other people to consider kidney donation, but also in the hope that hospitals might make the path for donors a little easier.

A breezy first step

I first offered my kidney to Ray at a party, after I had had a few drinks and was feeling expansive. Ray and his wife, Denise, had been telling me about Ray's kidney problems. He had been diagnosed with polycystic kidney disease about eight years earlier, and his kidney function was gradually deteriorating. His doctor had told him that he would ultimately need a kidney transplant. Denise would have donated one of hers, but she was not a good match, and their children were considered too young. Ray's only sister also had the disease.

I knew that I could manage perfectly well on one kidney and breezily offered him one of mine. He looked astonished at the idea and said very little. Later, I am afraid to say, I got cold feet. When I next saw Ray, I told him that my offer had been a joke and I had decided, if he didn't mind, to keep both my kidneys.

But then I began to think seriously about it and to discuss it with my husband and my two daughters, who are both in their 20s. Denise was a particularly old and valued friend. She and I had brought our children up together. My husband had been a junior doctor when our children were young, and during what felt like extremely long weekends when he was at the hospital for 72 hours at a stretch, I had taken my children round to Denise's house and spent many hours drinking tea while they played. She and Ray had provided what was almost a second home for them.

So when I discussed the idea with my family they were supportive, and I realised that it was not such a big step. I went back to Ray and told him that I was serious about the offer. I can remember his exact response: "I really don't know what to say."

Tests and delays

The next step was a trip to the Royal Free Hospital with Ray to be tested to see if I was a suitable donor. Rather to our astonishment, I turned out to be an excellent match.

There then began 16 months of tests, and it was during the last nine months of these that I became angry at what seemed to be unnecessary delays. I knew that I had to be thoroughly checked out for my own sake and the sake of the recipient, but I had naively thought that the hospital would be able to